

Applicant : Andica Biotech Inc. et al.
 Serial No. : 10/593,543
 Filed : September 20, 2006
 Page : 3 of 32

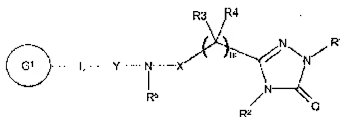
Attorney's File No.: 06275-833US1-10-41--P-US

Amendments to the Claims

This listing of claims replaces all prior versions and listings of claims in the application.

Listing of Claims

1. (Currently Amended) A compound of formula (I) or a pharmaceutically acceptable salt or solvate thereof



(I)

wherein

R¹ and R² independently represent H or C1 to 6 alkyl, said alkyl being optionally further substituted by an acyl ring or an aromatic heterocyclic ring containing 1 to 3 heteroatoms independently selected from O, S and N; said aromatic ring being optionally further substituted by halogen, CF₃, C1 to 4 alkyl or C1 to 4 alkoxy;

=> fil cap

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FILE COVERS 1907 - 12 Jan 2009 VOL 150 ISS 3
FILE LAST UPDATED: 11 Jan 2009 (20090111/ED)

Caplus now includes complete International Patent Classification (IPC) reclassification data for the third quarter of 2008.

Effective October 17, 2005, revised CAS Information Use Policies apply. They are available for your review at:

<http://www.cas.org/legal/infopolicy.html>

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L9

STR



C₁₉O
@19 20

VAR G1=H/15/16

REP G2=(1-3) 18

VAR G3=S/19

NODE ATTRIBUTES:

NSPEC IS RC AT 11

NSPEC IS RC AT 18

CONNECT IS E1 RC AT 15

DEFAULT MLEVEL IS ATOM

GGCAT IS SAT AT 15

GGCAT IS SAT AT 16

GGCAT IS UNS AT 17

DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED

NUMBER OF NODES IS 17

STEREO ATTRIBUTES: NONE

L11 35 SEA FILE=REGISTRY SSS FUL L9

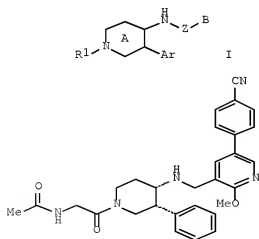
L12 10 SEA FILE=CAPLUS SPE=ON ABB=ON PLU=ON L11

=> d l12 ibib abs hitstr tot

L12 ANSWER 1 OF 10 CAPLUS COPYRIGHT 2009 ACS on STN
 ACCESSION NUMBER: 2007:874350 CAPLUS Full-text
 DOCUMENT NUMBER: 147:257652
 TITLE: Preparation of piperidine derivatives as tachykinin receptor antagonists
 INVENTOR(S): Shirai, Junya; Yoshikawa, Takeshi; Sugiyama, Hideyuki
 PATENT ASSIGNEE(S): Takeda Pharmaceutical Company Limited, Japan
 SOURCE: PCT Int. Appl., 133pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|--|----------|-----------------|----------|
| WO 2007089031 | A1 | 20070809 | WO 2007-JP52160 | 20070201 |
| W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW | | | |
| RW: | AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | |

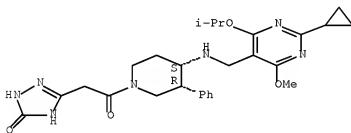
PRIORITY APPLN. INFO.: US 2006-763894P P 20060201
 OTHER SOURCE(S): MARPAT 147:257652
 GI



II

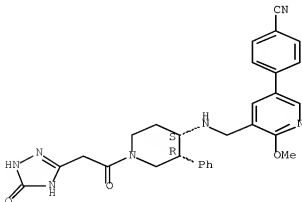
- AB Title compds. I [Ar = (un)substituted phenyl; R1 = H, (un)substituted hydrocarbyl, acyl or heterocyclyl; Z = (un)substituted methylene; ring A = (un)substituted piperidine; B = (un)substituted monocyclic aromatic heterocyclyl with provisions that substituents may form a ring], and their pharmaceutically acceptable salts, prodrugs are prepared and disclosed as tachykinin receptor antagonists and useful as an agent for the prophylaxis or treatment of lower urinary tract disease and the like. Thus, e.g., II was prepared by condensation of N-[2-((3R,4S)-4-amino-3-phenylpiperidin-1-yl)-2-oxoethyl]acetamide methanesulfonate (preparation given) with 4-(5-formyl-6-methoxypyridin-3-yl)benzonitrile (preparation given) followed by reduction. I have superior antagonistic activity, e.g., II showed IC50 value of 0.015 nM.
- IT 945954-65-4P 945954-79-0P
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (drug candidate; preparation of piperidine derivs. as tachykinin receptor antagonists)
- RN 945954-65-4 CAPLUS
- CN 3H-1,2,4-Triazol-3-one, 5-[2-[(3R,4S)-4-[[[2-cyclopropyl-4-methoxy-6-(1-methylethoxy)-5-pyrimidinyl]methyl]amino]-3-phenyl-1-piperidinyl]-2-oxoethyl]-1,2-dihydro- (CA INDEX NAME)

Absolute stereochemistry.



- RN 945954-79-0 CAPLUS
- CN Benzonitrile, 4-[5-[[[(3R,4S)-1-[2-(2,5-dihydro-5-oxo-1H-1,2,4-triazol-3-yl)acetyl]-3-phenyl-4-piperidinyl]amino]methyl]-6-methoxy-3-pyridinyl]- (CA INDEX NAME)

Absolute stereochemistry.



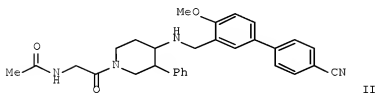
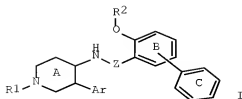
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 2 OF 10 CAPLUS COPYRIGHT 2009 ACS on STN
 ACCESSION NUMBER: 2007:705062 CAPLUS Full-text
 DOCUMENT NUMBER: 147:118148
 TITLE: Piperidine derivatives as tachykinin receptor antagonists and their preparation, pharmaceutical compositions and use in the treatment of lower urinary tract symptoms, gastrointestinal and central nerve disease
 INVENTOR(S): Ikeura, Yoshinori; Shirai, Junya; Yoshikawa, Takeshi; Sakauchi, Nobuki
 PATENT ASSIGNEE(S): Japan
 SOURCE: U.S. Pat. Appl. Publ., 89pp., Cont.-in-part of Appl. No. PCT/JP2006/315899.
 CODEN: USXXCO
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|------------------|----------|
| US 20070149570 | A1 | 20070628 | US 2007-701380 | 20070202 |
| WO 2007015588 | A1 | 20070208 | WO 2006-JP315899 | 20060804 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |

PRIORITY APPLN. INFO.: JP 2005-227183 A 20050804
 WO 2006-JP315899 A2 20060804

OTHER SOURCE(S): MARPAT 147:118148
 GI



AB The invention relates to a compound represented by formula I or a salt thereof. Compds. of formula I wherein Ar is (un)substituted Ph; R1 is H, (un)substituted hydrocarbon, acyl and (un)substituted heterocyclic group; R2 is H, (un)substituted C1-6 alkyl and (un)substituted C3-6 cycloalkyl; Z is (un)substituted methylene; ring A is a (un)substituted piperidine ring; ring B and ring C are (un)substituted benzene; R2 optionally form a ring together with the adjacent substituent on the ring B; and their salts thereof, are claimed. The compound of the invention has a superior tachykinin receptor antagonistic action, particularly a substance P receptor antagonistic action, and is useful as a pharmaceutical agent, for example, tachykinin receptor antagonist, an agent for the prophylaxis or treatment of lower urinary tract symptoms, gastrointestinal diseases or central nerve diseases. Example compound II was prepared by a general procedure (procedure given). All the invention compds. were evaluated for their tachykinin receptor antagonistic activity. From the assay, it was determined that compound II exhibited an IC50 value of 0.019 nM.

IT 923280-44-8P 923280-84-6P

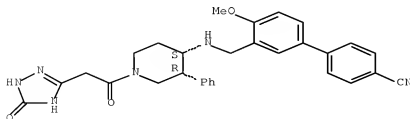
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(drug candidate; preparation of piperidine derivs. as tachykinin receptor antagonists and their use in the treatment of lower urinary tract symptoms, gastrointestinal and central nerve disease)

RN 923280-44-8 CAPLUS

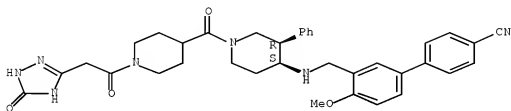
CN [1,1'-Biphenyl]-4-carbonitrile, 3'--[[[(3R,4S)-1-[2-(2,5-dihydro-5-oxo-1H-1,2,4-triazol-3-yl)acetyl]-3-phenyl-4-piperidinyl]amino]methyl]-4'-methoxy- (CA INDEX NAME)

Absolute stereochemistry.



RN 923280-84-6 CAPLUS
 CN [1,1'-Biphenyl]-4-carbonitrile, 3'-[[[(3R,4S)-1-[[1-(2-(2,5-dihydro-5-oxo-1H-1,2,4-triazol-3-yl)acetyl]-4-piperidinyl)carbonyl]-3-phenyl-4-piperidinyl]amino]methyl]-4'-methoxy-, hydrochloride (1:1) (CA INDEX NAME)

Absolute stereochemistry.



● HCl

L12 ANSWER 3 OF 10 CAPLUS COPYRIGHT 2009 ACS on STN
 ACCESSION NUMBER: 2007:485967 CAPLUS [Full-text](#)
 DOCUMENT NUMBER: 146:482087
 TITLE: Preparation of heterocyclic amide compounds as matrix metalloproteinase inhibitors
 INVENTOR(S): Nara, Hiroshi; Kaieda, Akira; Sato, Kenjiro; Terauchi, Jun
 PATENT ASSIGNEE(S): Takeda Pharmaceutical Company Limited, Japan
 SOURCE: PCT Int. Appl., 330pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: Japanese
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|--|----------|------------------|----------|
| WO 2007049820 | A1 | 20070503 | WO 2006-JP322043 | 20061027 |
| W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW | | | |
| RW: | AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | |
| AU 2006306991 | A1 | 20070503 | AU 2006-306991 | 20061027 |
| CA 2627497 | A1 | 20070503 | CA 2006-2627497 | 20061027 |
| EP 1953148 | A1 | 20080806 | EP 2006-822961 | 20061027 |

R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
IS, IT, LI, LT, LU, LV, MC, NL, PL, RO, SE, SI, SK, TR, AL,
BA, HR, MK, RS

MX 200805416

A

20080512

MX 2008-5416

20080425

KR 2008066061

A

20080715

KR 2008-712886

20080528

PRIORITY APPLN. INFO.:

JP 2005-315267

A 20051028

WO 2006-JP22043

W 20061027

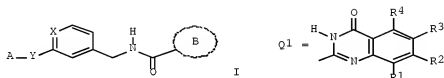
WO 2006-JP322043

W 20061027

OTHER SOURCE(S):

MARPAT 146:482087

GI



AB The title compds. I [A = zinc-bonding group; X = CZ, N; Z = H, halo; Y = (un)substituted spacer having 2 to 10 atoms; ring B = Q1, etc.; R1 - R4 = H, halo, cyano, etc.; excluding 6 specific compds.] are prepared Thus, 4-oxo-N-[3-((2-((1H-1,2,4-triazol-3-ylthio)ethyl)oxy)phenyl)methyl]-3,4-dihydroquinazoline-2-carboxamide was prepared in several steps starting from 3-hydroxybenzonitrile and 1-bromo-2-chloroethane. In an in vitro assay, compds. of this invention at 1 μ M gave 81% to 100% inhibition of matrix metalloproteinase 13. Formulations are given.

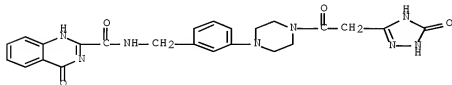
IT 935759-87-8P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of heterocyclic amide compds. as matrix metalloproteinase inhibitors)

RN 935759-87-8 CAPLUS

CN 2-Quinazolinecarboxamide, N-[[3-[4-[2-(2,5-dihydro-5-oxo-1H-1,2,4-triazol-3-yl)acetyl]-1-piperazinyl]phenyl)methyl]-3,4-dihydro-4-oxo- (CA INDEX NAME)



REFERENCE COUNT:

5

THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 4 OF 10 CAPLUS COPYRIGHT 2009 ACS ON STN

ACCESSION NUMBER: 2007:150254 CAPLUS [Full-text](#)

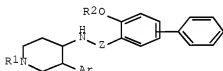
DOCUMENT NUMBER: 146:206214

TITLE: Preparation of biphenylmethylaminopiperidines as

tachykinin receptor antagonists.
 Ikeura, Yoshinori; Shirai, Junya; Yoshikawa, Takeshi;
 Sakauchi, Nobuki
 Takeda Pharmaceutical Company Limited, Japan
 PCT Int. Appl., 174pp.
 CODEN: PIXXD2
 Patent
 English
 FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|------|----------|------------------|----------|
| WO 2007015588 | A1 | 20070208 | WO 2006-JP315899 | 20060804 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM EP 1910292 A1 20080416 EP 2006-782685 20060804 R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR US 20070149570 A1 20070628 US 2007-701380 20070202 JP 2005-227183 A 20050804 WO 2006-JP315899 W 20060804 | | | | |
| PRIORITY APPLN. INFO.: | | | | |

OTHER SOURCE(S): MARPAT 146:206214
 GI



I

AB Title compds. [I; Ar = (substituted) Ph; R1 = H, (substituted) hydrocarbyl, acyl, heterocyclyl; R2 = H, (substituted) alkyl, cycloalkyl; Z = (alkyl-substituted) methylene; all rings may be further substituted; with 2 specifically excluded compds.], were prepared Thus, N-[2-[(3R,4S)-4-[[4'-(ethynyl)-4-methoxybiphenyl-3-yl)methyl]amino]-3- phenylpiperidin-1-yl]-2-oxoethylacetamide (general preparation given) showed radioligand receptor binding inhibitory activity in IM-9 human lymphoblast cells with IC50 = 0.015 nM.

IT 923280-44-3P 923280-84-6P

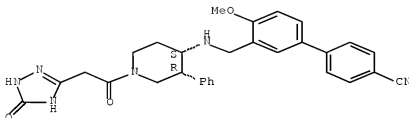
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of biphenylmethylaminopiperidines as tachykinin receptor antagonists)

RN 923280-44-8 CAPLUS

CN [1,1'-Biphenyl]-4-carbonitrile, 3'--[[(3R,4S)-1-[2-(2,5-dihydro-5-oxo-1H-1,2,4-triazol-3-yl)acetyl]-3-phenyl-4-piperidinyl]amino]methyl]-4'-methoxy- (CA INDEX NAME)

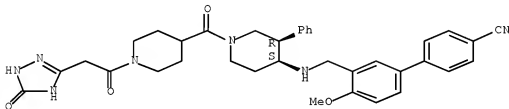
Absolute stereochemistry.



RN 923280-84-6 CAPLUS

CN [1,1'-Biphenyl]-4-carbonitrile, 3'--[[(3R,4S)-1-[1-[2-(2,5-dihydro-5-oxo-1H-1,2,4-triazol-3-yl)acetyl]-4-piperidinyl]carbonyl]-3-phenyl-4-piperidinyl]amino]methyl]-4'-methoxy-, hydrochloride (1:1) (CA INDEX NAME)

Absolute stereochemistry.



● HCl

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 5 OF 10 CAPLUS COPYRIGHT 2009 ACS ON STN

ACCESSION NUMBER: 2006:1155411 CAPLUS Full-text

DOCUMENT NUMBER: 145:471540

TITLE: Preparation of piperidine derivatives as tachykinin receptor antagonists

INVENTOR(S): Nagaoka, Naomi; Marunaka, Shigeyuki; Fukuta, Makoto

PATENT ASSIGNEE(S): Takeda Pharmaceutical Company Limited, Japan

SOURCE: PCT Int. Appl., 323pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|------|----------|------------------|----------|
| WO 2006115285 | A1 | 20061102 | WO 2006-JP308919 | 20060421 |
| <p>W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW</p> <p>RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM</p> | | | | |

PRIORITY APPLN. INFO.: JP 2005-124335 A 20050421

OTHER SOURCE(S): MARPAT 145:471540

AB The title compds. (no biol. data) are prepared This document discloses a pharmaceutical composition comprising N-(2-[(3R,4S)-4-((2-methoxy-5-[5-(trifluoromethyl)-1H-tetrazol-1-yl]benzyl)amino)-3-phenylpiperidin-1-yl]-2-oxoethyl)acetamide (I), a salt or a prodrug thereof, a sugar and a hydrophilic water-insol. substance. Thus, N-(2-[(3R,4S)-4-((2-hydroxy-5-[5-(trifluoromethyl)-1H-tetrazol-1-yl]benzyl)amino)-3-phenylpiperidin-1-yl]-2-oxoethyl)acetamide was prepared in 3 steps from (3R,4S)-4-amino-3-phenylpiperidine-1-carboxylic acid tert-Bu ester and 2-hydroxy-5-[5-(trifluoromethyl)-1H-tetrazol-1-yl]benzaldehyde. Formulations containing I are given. Tablets containing I showed high elution stability.

IT 632352-46-6P

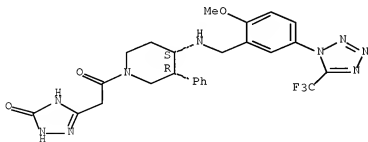
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of piperidine derivs. as tachykinin receptor antagonists)

RN 632352-46-6 CAPLUS

CN 3H-1,2,4-Triazol-3-one, 1,2-dihydro-5-[2-[(3R,4S)-4-[[2-methoxy-5-[5-(trifluoromethyl)-1H-tetrazol-1-yl]phenyl]methyl]amino]-3-phenyl-1-piperidinyl]-2-oxoethyl]-, rel- (CA INDEX NAME)

Relative stereochemistry.



REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 6 OF 10 CAPLUS COPYRIGHT 2009 ACS ON STN
 ACCESSION NUMBER: 2006:272922 CAPLUS [Full-text](#)
 DOCUMENT NUMBER: 144:331270

TITLE: Preparation of piperidine derivatives as tachykinin receptor antagonists

INVENTOR(S): Ikeura, Yoshinori; Hashimoto, Tadatosh; Nishida, Haruyuki; Shirai, Junya; Sakauchi, Nobuki

PATENT ASSIGNEE(S): Takeda Pharmaceutical Company Limited, Japan

SOURCE: PCT Int. Appl., 222 pp.
CODEN: PIXXD2

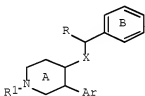
DOCUMENT TYPE: Patent

LANGUAGE: Japanese

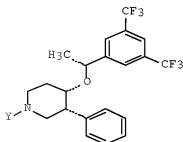
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|--|-------------------|-----------------|------------|
| WO 2006030975 | A1 | 20060323 | WO 2005-JP17538 | 20050916 |
| W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | |
| RW: | AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | |
| EP 1790636 | A1 | 20070530 | EP 2005-785870 | 20050916 |
| R: | AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR | | | |
| US 20060142337 | A1 | 20060629 | US 2006-358070 | 20060222 |
| PRIORITY APPLN. INFO.: | | | JP 2004-272639 | A 20040917 |
| | | | WO 2005-JP17538 | W 20050916 |
| OTHER SOURCE(S): | | MARPAT 144:331270 | | |
| GI | | | | |



I



II

AB Title compds. I [Ar = (un)substituted aryl; R = alkyl; R1 = H, (un)substituted hydrocarbon, acyl, etc.; X = O, (un)substituted imino; ring A = piperidine ring which may have an addnl. substituent; ring B = substituted benzene] were prepared. For example, compound II [Y = H]·HCl was prepared from (3R,4S)-4-hydroxy-3-phenylpiperidine-1-carboxylic acid tert-Bu ester in a multistep process. In radioligand receptor binding inhibition assays, compound II [Y = (1-acetylpiperidin-4-yl)carbonyl] exhibited the IC50 value of 0.026 nM. Compds. I are claimed useful for the treatment of irritable bowel disease, depression, etc.

IT 880092-22-8P 880092-48-8P 880092-69-7P

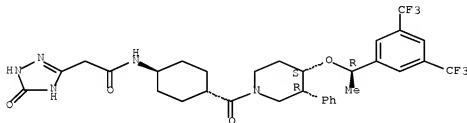
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of piperidine derivs. as tachykinin receptor antagonists for treatment of irritable bowel disease, depression, etc.)

RN 880092-22-8 CAPLUS

CN 1H-1,2,4-Triazole-3-acetamide, N-[trans-4-[(3R,4S)-4-[(1R)-1-[3,5-bis(trifluoromethyl)phenyl]ethoxy]-3-phenyl-1-piperidinyl]carbonyl]cyclohexyl]-2,5-dihydro-5-oxo- (CA INDEX NAME)

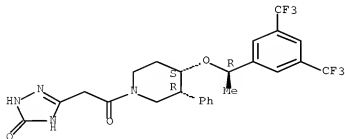
Absolute stereochemistry.



RN 880092-48-8 CAPLUS

CN 3H-1,2,4-Triazol-3-one, 5-[2-[(3R,4S)-4-[(1R)-1-[3,5-bis(trifluoromethyl)phenyl]ethoxy]-3-phenyl-1-piperidinyl]-2-oxoethyl]-1,2-dihydro- (CA INDEX NAME)

Absolute stereochemistry.

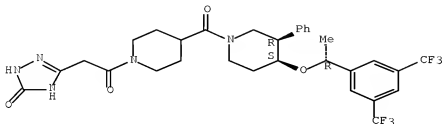


RN 880092-89-7 CAPLUS

CN 3H-1,2,4-Triazol-3-one, 5-[2-[4-[(3R,4S)-4-[(1R)-1-[3,5-bis(trifluoromethyl)phenyl]ethoxy]-3-phenyl-1-piperidinyl]carbonyl]-1-

piperidinyl]-2-oxoethyl]-1,2-dihydro- (CA INDEX NAME)

Absolute stereochemistry.

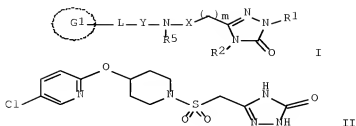


REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 7 OF 10 CAPLUS COPYRIGHT 2009 ACS ON STN
 ACCESSION NUMBER: 2005:1106854 CAPLUS [Full-text](#)
 DOCUMENT NUMBER: 143:387043
 TITLE: Preparation of triazolone derivatives as MMP inhibitors for the treatment of asthma
 INVENTOR(S): Eriksson, Anders; Lepistoe, Matti
 PATENT ASSIGNEE(S): Astrazeneca AB, Swed.
 SOURCE: PCT Int. Appl., 53 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|--|----------|------------------|------------|
| WO 2005095362 | A1 | 20051013 | WO 2005-SE448 | 20050329 |
| W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | |
| RW: | BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | |
| EP 1732903 | A1 | 20061220 | EP 2005-722275 | 20050329 |
| R: | AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR | | | |
| CN 1960979 | A | 20070509 | CN 2005-80017672 | 20050329 |
| JP 2007530672 | T | 20071101 | JP 2007-506108 | 20050329 |
| US 20070219217 | A1 | 20070920 | US 2006-593543 | 20060920 |
| IN 2006DN05541 | A | 20070803 | IN 2006-DN5541 | 20060922 |
| PRIORITY APPLN. INFO.: | | | SE 2004-850 | A 20040330 |
| | | | WO 2005-SE448 | W 20050329 |

OTHER SOURCE(S): CASREACT 143:387043; MARPAT 143:387043
 GI

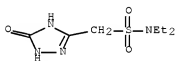


AB Title compds. represented by the formula I [wherein R1, R2 = independently H, Cl or (un)substituted alkyl; R3, R4 = independently H, Cl, (un)substituted alkyl or R3R4 = (hetero)cyclyl; m = 1-3; X = SO, SO2 or CO; R5 = H, Cl or (un)substituted alkyl; Y = a direct bond or NR5Y = azacyclic ring; L = a direct bond, O, amino, etc.; G1 = (un)substituted cyclic ring; and pharmaceutically acceptable salts or solvates thereof] were prepared as metalloproteinase (MMP) inhibitors. For example, II was provided in a multi-step synthesis starting from the reaction of 5-(chloromethyl)-2,4-dihydro-3H-1,2,4-triazol-3-one with benzyl mercaptan. I and their pharmaceutical compns. are useful as MMP inhibitors for the treatment of asthma or other MMP-12 and/or MMP-9 mediated diseases (no data).

IT 866602-62-2E, N,N-Diethyl-1-(5-oxo-4,5-dihydro-1H-1,2,4-triazol-3-yl)methanesulfonamide
 RL: BYP (Byproduct); PREP (Preparation)
 (preparation of triazolone derivs. as MMP inhibitors for treatment of asthma)

RN 866602-62-2 CAPLUS

CN 1H-1,2,4-Triazol-3-one 866602-62-2E, N,N-diethyl-2,5-dihydro-5-oxo- (CA INDEX NAME)

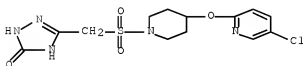


IT 866602-59-7E, 5-[[[4-[(5-Chloropyridin-2-yl)oxy]piperidin-1-yl]sulfonyl]methyl]-2,4-dihydro-3H-1,2,4-triazol-3-one
 866602-63-3E, 5-[2-[[4-[(5-Chloropyridin-2-yl)oxy]piperidin-1-yl]sulfonyl]ethyl]-2,4-dihydro-3H-1,2,4-triazol-3-one 866602-67-7E
 , 5-[3-[[4-[(5-Chloropyridin-2-yl)oxy]piperidin-1-yl]sulfonyl]propyl]-2,4-dihydro-3H-1,2,4-triazol-3-one 866602-71-3E,
 5-[[[4-(4-Chlorophenyl)piperazin-1-yl]sulfonyl]methyl]-2,4-dihydro-3H-1,2,4-triazol-3-one 866602-72-4E,
 5-[[[4-[(2-Methoxy-5-pyrimidin-5-yl)ethynyl]-3,6-dihydropyridin-1(2H)-yl]sulfonyl]methyl]-2,4-dihydro-3H-1,2,4-triazol-3-one
 866602-73-5E, 5-[[[4-[[2-(Trifluoromethyl)pyrimidin-5-yl]ethynyl]-3,6-dihydropyridin-1(2H)-yl]sulfonyl]methyl]-2,4-dihydro-3H-1,2,4-triazol-3-one 866602-74-6E, 5-[[[4-[(2-Cyclopropylpyrimidin-5-yl)ethynyl]-3,6-dihydropyridin-1(2H)-yl]sulfonyl]methyl]-2,4-dihydro-3H-

1,2,4-triazol-3-one 866602-75-7F,
 5-[[[4-(4-Chlorophenyl)piperidin-1-yl]sulfonyl]methyl]-2,4-dihydro-3H-
 1,2,4-triazol-3-one 866602-76-8F,
 N-Benzyl-1-(5-oxo-4,5-dihydro-1H-1,2,4-triazol-3-yl)methanesulfonamide
 866602-77-9F, 1-(5-Oxo-4,5-dihydro-1H-1,2,4-triazol-3-yl)-N-(2-
 phenylethyl)methanesulfonamide 866602-78-0F,
 5-[2-[[4-(4-Chlorophenyl)piperidin-1-yl]sulfonyl]ethyl]-2,4-dihydro-3H-
 1,2,4-triazol-3-one 866602-79-1F,
 5-[2-[[4-(4-Chlorophenyl)piperazin-1-yl]sulfonyl]ethyl]-2,4-dihydro-3H-
 1,2,4-triazol-3-one 866602-80-4F,
 5-[3-[[4-(4-Chlorophenyl)piperidin-1-yl]sulfonyl]propyl]-2,4-dihydro-3H-
 1,2,4-triazol-3-one 866602-81-5F,
 5-[3-[[4-(4-Chlorophenyl)piperazin-1-yl]sulfonyl]propyl]-2,4-dihydro-3H-
 1,2,4-triazol-3-one
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
 (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
 (Uses)
 (preparation of triazolone derivs. as MMP inhibitors for treatment of
 asthma)

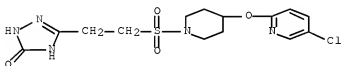
RN 866602-59-7 CAPLUS

CN 3H-1,2,4-Triazol-3-one, 5-[[[4-[(5-chloro-2-pyridinyl)oxy]-1-
 piperidinyl]sulfonyl]methyl]-1,2-dihydro- (CA INDEX NAME)



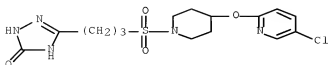
RN 866602-63-3 CAPLUS

CN 3H-1,2,4-Triazol-3-one, 5-[2-[[4-[(5-chloro-2-pyridinyl)oxy]-1-
 piperidinyl]sulfonyl]ethyl]-1,2-dihydro- (CA INDEX NAME)



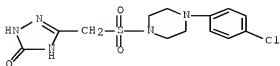
RN 866602-67-7 CAPLUS

CN 3H-1,2,4-Triazol-3-one, 5-[3-[[4-[(5-chloro-2-pyridinyl)oxy]-1-
 piperidinyl]sulfonyl]propyl]-1,2-dihydro- (CA INDEX NAME)



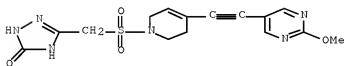
RN 866602-71-3 CAPLUS

CN 3H-1,2,4-Triazol-3-one, 5-[[[4-(4-chlorophenyl)-1-piperazinyl]sulfonyl]methyl]-1,2-dihydro- (CA INDEX NAME)



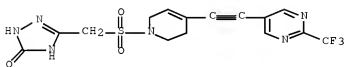
RN 866602-72-4 CAPLUS

CN 3H-1,2,4-Triazol-3-one, 5-[[[3,6-dihydro-4-[2-(2-methoxy-5-pyrimidinyl)ethynyl]-1(2H)-pyridinyl]sulfonyl]methyl]-1,2-dihydro- (CA INDEX NAME)



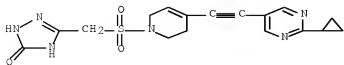
RN 866602-73-5 CAPLUS

CN 3H-1,2,4-Triazol-3-one, 5-[[[3,6-dihydro-4-[2-[2-(trifluoromethyl)-5-pyrimidinyl]ethynyl]-1(2H)-pyridinyl]sulfonyl]methyl]-1,2-dihydro- (CA INDEX NAME)



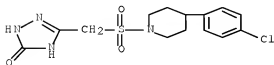
RN 866602-74-6 CAPLUS

CN 3H-1,2,4-Triazol-3-one, 5-[[[4-[2-(2-cyclopropyl-5-pyrimidinyl)ethynyl]-3,6-dihydro-1(2H)-pyridinyl]sulfonyl]methyl]-1,2-dihydro- (CA INDEX NAME)



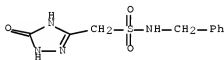
RN 866602-75-7 CAPLUS

CN 3H-1,2,4-Triazol-3-one, 5-[[[4-(4-chlorophenyl)-1-piperidinyl]sulfonyl]methyl]-1,2-dihydro- (CA INDEX NAME)



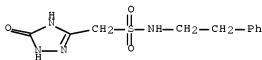
RN 866602-76-8 CAPLUS

CN 1H-1,2,4-Triazole-3-methanesulfonamide, 2,5-dihydro-5-oxo-N-(phenylmethyl)- (CA INDEX NAME)



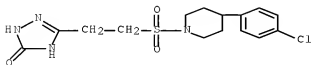
RN 866602-77-9 CAPLUS

CN 1H-1,2,4-Triazole-3-methanesulfonamide, 2,5-dihydro-5-oxo-N-(2-phenylethyl)- (CA INDEX NAME)



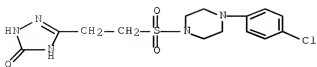
RN 866602-78-0 CAPLUS

CN 3H-1,2,4-Triazol-3-one, 5-[2-[[4-(4-chlorophenyl)-1-piperidinyl]sulfonyl]ethyl]-1,2-dihydro- (CA INDEX NAME)

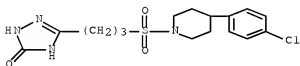


RN 866602-79-1 CAPLUS

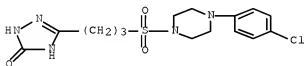
CN 3H-1,2,4-Triazol-3-one, 5-[2-[[4-(4-chlorophenyl)-1-piperazinyl]sulfonyl]ethyl]-1,2-dihydro- (CA INDEX NAME)



RN 866602-80-4 CAPLUS
 CN 3H-1,2,4-Triazol-3-one, 5-[3-[[4-(4-chlorophenyl)-1-piperidinyl]sulfonyl]propyl]-1,2-dihydro- (CA INDEX NAME)



RN 866602-81-5 CAPLUS
 CN 3H-1,2,4-Triazol-3-one, 5-[3-[[4-(4-chlorophenyl)-1-piperazinyl]sulfonyl]propyl]-1,2-dihydro- (CA INDEX NAME)



REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 8 OF 10 CAPLUS COPYRIGHT 2009 ACS ON STN

ACCESSION NUMBER: 2003:972057 CAPLUS [Full-text](#)

DOCUMENT NUMBER: 140:27765

TITLE: Preparation of piperidine derivatives as tachykinin receptor antagonists for treatment of frequent urination and urinary incontinence

INVENTOR(S): Ikeura, Yoshinori; Hashimoto, Tadatoshi; Tarui, Naoki; Shirai, Junya; Yamashita, Masayuki

PATENT ASSIGNEE(S): Takeda Chemical Industries, Ltd., Japan

SOURCE: PCT Int. Appl., 264 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.

KIND DATE

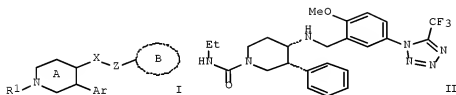
APPLICATION NO.

DATE

| | | | | |
|------------------------|--|----------|-----------------|------------|
| WO 2003101964 | A1 | 20031211 | WO 2003-JP6754 | 20030529 |
| W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LI, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | |
| RW: | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | |
| CA 2487688 | A1 | 20031211 | CA 2003-2487688 | 20030529 |
| AU 2003241903 | A1 | 20031219 | AU 2003-241903 | 20030529 |
| BR 2003011425 | A | 20050315 | BR 2003-11425 | 20030529 |
| EP 1553084 | A1 | 20050713 | EP 2003-733151 | 20030529 |
| R: | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | |
| CN 1671662 | A | 20050921 | CN 2003-818354 | 20030529 |
| NZ 537330 | A | 20070427 | NZ 2003-537330 | 20030529 |
| JP 2004285038 | A | 20041014 | JP 2003-154345 | 20030530 |
| MX 2004PA11730 | A | 20050714 | MX 2004-PA11730 | 20041125 |
| US 20060167052 | A1 | 20060727 | US 2004-516252 | 20041129 |
| ZA 2004010085 | A | 20060726 | ZA 2004-10085 | 20041214 |
| IN 2004KN01942 | A | 20061201 | IN 2004-KN1942 | 20041216 |
| NO 2004005701 | A | 20050216 | NO 2004-5701 | 20041229 |
| PRIORITY APPLN. INFO.: | | | JP 2002-159338 | A 20020531 |
| | | | JP 2003-17885 | A 20030127 |
| | | | WO 2003-JP6754 | W 20030529 |

OTHER SOURCE(S): MARPAT 140:27765

GI



AB The title compds. I [wherein Ar = (un)substituted aryl, aralkyl, or heteroaryl; R1 = H, acyl, (un)substituted hydrocarbyl, or heterocyclyl; X = O or (un)substituted NH; Z = (un)substituted CH2; ring A = (un)substituted piperidine; ring B = (un)substituted aryl; with exclusions] or prodrugs or salts thereof are prepared I have excellent tachykinin receptor antagonistic activity, and are useful for the treatment of frequent urination and urinary incontinence (no data). For example, the compound II•xHCl was prepared in a multi-step synthesis. II showed antagonistic activity with IC50 of 0.025 nM against human substance P receptor. Formulations containing I as an active ingredient were also described.

IT 633352-46-6P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

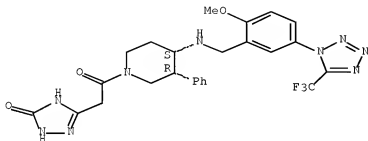
(drug candidate; preparation of piperidine derivs. as tachykinin receptor

antagonists for treatment of frequent urination and urinary incontinence)

RN 632352-46-6 CAPLUS

CN 3H-1,2,4-Triazol-3-one, 1,2-dihydro-5-[2-[(3R,4S)-4-[[[2-methoxy-5-[5-(trifluoromethyl)-1H-tetrazol-1-yl]phenyl]methyl]amino]-3-phenyl-1-piperidinyl]-2-oxoethyl]-, rel- (CA INDEX NAME)

Relative stereochemistry.



REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 9 OF 10 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1988:492870 CAPLUS [Full-text](#)

DOCUMENT NUMBER: 109:92870

ORIGINAL REFERENCE NO.: 109:15497a,15500a

TITLE: Synthesis of azoles and fused azoles from

α -arylhydrazononitriles

AUTHOR(S): Ibrahim, Mohamed Kamal Ahmed; El-Moghayar, Mohamed Riffat Hamza

CORPORATE SOURCE: Fac. Sci., Cairo Univ., Giza, Egypt

SOURCE: Indian Journal of Chemistry, Section B: Organic Chemistry Including Medicinal Chemistry (1987), 26B(9), 832-5

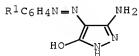
CODEN: IJSBDB; ISSN: 0376-4699

DOCUMENT TYPE: Journal

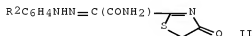
LANGUAGE: English

OTHER SOURCE(S): CASREACT 109:92870

GI



I



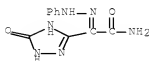
II

AB Cyanoacetamides $R_1C_6H_4NHN:C(CONH_2)CN$ ($R_1 = H, Me, Cl$) were heated with N_2H_4 to give pyrazoles I. Also prepared, from cyanoacetamides and $HSCH_2CO_2H$, were thiazolinones II ($R_2 = Cl, CO_2H$).

IT 115998-45-3P

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 115998-45-3 CAPLUS

CN 1H-1,2,4-Triazole-3-acetamide, 2,5-dihydro-5-oxo- α -(2-phenylhydrazinylidene)- (CA INDEX NAME)

L12 ANSWER 10 OF 10 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1977:468245 CAPLUS [Full-text](#)

DOCUMENT NUMBER: 87:68245

ORIGINAL REFERENCE NO.: 87:10865a,10868a

TITLE: Structural elucidation of the reaction products from

benzonitrile oxide and 1,4-disubstituted urazoles

Hoyer, Georg A.; Boroschewski, Gerhard

CORPORATE SOURCE: Forschungslab., Schering A.-G., Berlin, Fed. Rep. Ger.

SOURCE: Archiv der Pharmazie (Weinheim, Germany) (1977),

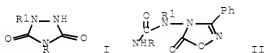
310(3), 255-9

CODEN: ARPMA5; ISSN: 0365-6233

DOCUMENT TYPE: Journal

LANGUAGE: German

GI



AB The reaction of benzonitrile oxide with urazoles (I; R = R₁ = Me; R = Ph, R₁ = Me; R = Me, R₁ = Ph; R = R₁ = Ph) does not yield the corresponding 1,4-disubstituted 3-(phenylcarbamoyloxy)- Δ^2 -1,2,4-triazolin-5-ones as previously reported (Sunderdiek, R. et al, 1974), but leads to oxadiazolinones (II; R, R₁ as above).

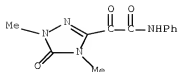
IT 53425-53-6

RL: RCT (Reactant); RACT (Reactant or reagent)

(oxadiazolinones vs., as reaction products of benzonitrile oxide and urazoles)

RN 63425-53-6 CAPLUS

CN 1H-1,2,4-Triazole-3-acetamide, 4,5-dihydro-1,4-dimethyl- α ,5-dioxo-N-phenyl- (CA INDEX NAME)



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=> fil cap dissabs confsci wpix
FILE 'CAPLUS' ENTERED AT 11:06:19 ON 12 JAN 2009
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FILE 'CONFSCI' ENTERED AT 11:06:19 ON 12 JAN 2009
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FILE 'WPIX' ENTERED AT 11:06:19 ON 12 JAN 2009
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=> d que 123
L19      496 SEA ERIKSSON A/AU OR ERIKSSON ANDER?/AU
L20      38 SEA LEPISTO M/AU OR LEPISTO M ?/AU OR LEPISTO MATT?/AU
L21      613 SEA L19 OR ERIKSSON A ?/AU
L22      643 SEA (L20 OR L21)
L23      7 SEA L22 AND TRIAZOL?

=> dup rem 123
PROCESSING COMPLETED FOR L23
L24      5 DUP REM L23 (2 DUPLICATES REMOVED)
          ANSWERS '1-4' FROM FILE CAPLUS
          ANSWER '5' FROM FILE WPIX

=> d 124 ibib abs tot

L24 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 1
ACCESSION NUMBER: 2005:1106854 CAPLUS Full-text
DOCUMENT NUMBER: 143:387043
TITLE: Preparation of triazolone derivatives as MMP
inhibitors for the treatment of asthma
Eriksson, Anders; Lepistoe, Matti
INVENTOR(S): Astrazeneca AB, Swed.
PATENT ASSIGNEE(S): Astrazeneca AB, Swed.
SOURCE: PCT Int. Appl., 53 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:
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| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|------|----------|-----------------|----------|
| WO 2005095362 | A1 | 20051013 | WO 2005-SE448 | 20050329 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, | | | | |

CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
 RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

EP 1732903 A1 20061220 EP 2005-722275 20050329

R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR

CN 1960979 A 20070509 CN 2005-80017672 20050329

JP 2007530672 T 20071101 JP 2007-506108 20050329

US 20070219217 A1 20070920 US 2006-593543 20060920

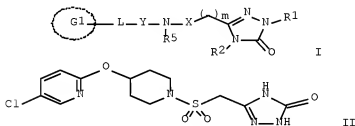
IN 2006DN05541 A 20070803 IN 2006-DN5541 20060922

PRIORITY APPLN. INFO.: SE 2004-850 A 20040330

WO 2005-SE448 W 20050329

OTHER SOURCE(S): CASREACT 143:387043; MARPAT 143:387043

GI



AB Title compds. represented by the formula I [wherein R1, R2 = independently H, Cl or (un)substituted alkyl; R3, R4 = independently H, Cl, (un)substituted alkyl or R3R4 = (hetero)cyclyl; m = 1-3; X = SO, SO2 or CO; R5 = H, Cl or (un)substituted alkyl; Y = a direct bond or NR5Y = azacyclic ring; L = a direct bond, O, amino, etc.; G1 = (un)substituted cyclic ring; and pharmaceutically acceptable salts or solvates thereof] were prepared as metalloproteinase (MMP) inhibitors. For example, II was provided in a multi-step synthesis starting from the reaction of 5-(chloromethyl)-2,4-dihydro-3H-1,2,4-triazol-3-one with benzyl mercaptan. I were tested for inhibition of human MMP12, MMP9, MMP2, MMP19, MMP14 and MMP8. I and their pharmaceutical compds. are useful as MMP inhibitors for the treatment of asthma or other MMP-12 and/or MMP-9 mediated diseases (no data).

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 2

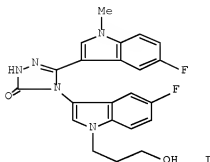
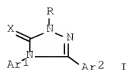
ACCESSION NUMBER: 2000:842129 CAPLUS Full-text

DOCUMENT NUMBER: 134:29418

TITLE: Preparation of New triazoles as pharmaceutically active compounds activity as kinase inhibitors

INVENTOR(S): Karabelas, Kostas; Lepisto, Matti; Sjo, Peter
 PATENT ASSIGNEE(S): AstraZeneca AB, Swed.
 SOURCE: PCT Int. Appl., 127 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------------------|----------|-----------------|------------|
| WO 2000071537 | A1 | 20001130 | WO 2000-SE1009 | 20000519 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2372743 | A1 | 20001130 | CA 2000-2372743 | 20000519 |
| BR 2000010520 | A | 20020219 | BR 2000-10520 | 20000519 |
| EP 1183252 | A1 | 20020306 | EP 2000-931873 | 20000519 |
| EP 1183252 | B1 | 20040218 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, MC, PT, IE, SI, LT, LV, FI, RO | | | | |
| JP 2003500404 | T | 20030107 | JP 2000-619794 | 20000519 |
| NZ 515281 | A | 20030829 | NZ 2000-515281 | 20000519 |
| AT 259798 | T | 20040315 | AT 2000-931873 | 20000519 |
| US 6492406 | B1 | 20021210 | US 2000-646972 | 20000925 |
| ZA 2001009049 | A | 20030203 | ZA 2001-9049 | 20011101 |
| NO 2001005664 | A | 20020121 | NO 2001-5664 | 20011120 |
| MX 2001PA11884 | A | 20020506 | MX 2001-PA11884 | 20011121 |
| PRIORITY APPLN. INFO.: | | | SE 1999-1854 | A 19990521 |
| | | | SE 2000-645 | A 20000228 |
| | | | WO 2000-SE1009 | W 20000519 |
| OTHER SOURCE(S): | MARPAT 134:29418 | | | |
| GI | | | | |



AB Title compds. [I; wherein one of Ar and Ar is optionally substituted bicyclic heteroaryl or optionally substituted tricyclic heteroaryl and the other is optionally substituted heteroaryl or optionally substituted aryl; X is O or S; and R is H, OH, NH or C alkyl (itself optionally substituted by amino or hydroxyl), stereoisomers, salts, and solvates which are protein kinase C inhibitors are prepared and pharmaceutical compds. comprising them are useful to include prophylactic, diagnostic and therapeutic regimens carried out in vivo or ex vivo on humans or other mammals. Thus, the title compound II was prepared

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2009 ACS on SIN

ACCESSION NUMBER: 2008:771134 CAPLUS [Full-text](#)

DOCUMENT NUMBER: 149:104697

TITLE: Indazolyl ester and amide derivatives for the treatment of glucocorticoid receptor mediated disorders and their preparation

INVENTOR(S): Berger, Markus; Dahmen, Jan; Eriksson, Anders; Gabos, Balint; Hansson, Thomas; Hemmerling, Martin; Henriksson, Krister; Ivanova, Svetlana; Lepistoe, Matti; McKerrecher, Darren; Munck Af Rosenschold, Magnus; Nilsson, Stinabritt; Rehwinkel, Hartmut; Taflin, Camilla

PATENT ASSIGNEE(S): Astrazeneca AB, Swed.; Bayer Schering Pharma Aktiengesellschaft

SOURCE: PCT Int. Appl., 310pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

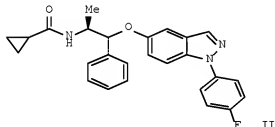
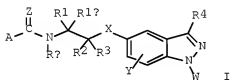
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|------|----------|-----------------|----------|
| WO 2008076048 | A1 | 20080626 | WO 2007-SE1136 | 20071220 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, | | | | |

CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI,
 GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG,
 KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME,
 MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL,
 PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN,
 TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
 RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
 IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF,
 BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW,
 GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,
 BY, KG, KZ, MD, RU, TJ, TM

| | | | | |
|------------------------|----|----------|-----------------|------------|
| US 20080214641 | A1 | 20080904 | US 2007-5066 | 20071220 |
| PRIORITY APPLN. INFO.: | | | US 2006-871184P | P 20061221 |
| | | | US 2007-941745P | P 20070604 |
| | | | US 2007-978526P | P 20071009 |

OTHER SOURCE(S): MARPAT 149:104697

GI



AB The present invention relates to indazolyl ester or amide derivs. of formula I, to pharmaceutical compns. comprising such derivs., to processes for preparing such novel derivs. and to the use of such derivs. as medicaments. Compds. of formula I wherein A is C1-6 (hydroxy)alkyl, C1-6 cyanoalkyl, CN, C1-6 nitroalkyl, NO2, C1-6 alkoxy, etc.; Rx is H; RxA taken together to form azacyclic ring; R1 and R1a is H, C1-4 (hydroxy)alkyl, C1-4 alkyl-O-C1-4 alkyl, C1-4 alkyl-S-C1-4 alkyl, C1-4 haloalkyl; R1R1a taken together to form oxo; R2 is H and C1-4 alkyl; R3 is (un)substituted C5-10 aryl(oxy), (un)substituted C5-10 aryl-C1-4 alkyl, (un)substituted C5-10 aryloxy-C1-4 alkyl and (un)substituted C5-10 heteroaryl; R4 is H, OH, halo, and C1-4 (halo)alkyl; W is H, (un)substituted Ph, (un)substituted C1-4 alkyl, (un)substituted C3-7 cycloalkyl, (un)substituted thienyl, (un)substituted isoxazolyl, (un)substituted pyrazolyl, (un)substituted pyridinyl, (un)substituted pyridazinyl, and (un)substituted pyrimidinyl; X is CH2, O, S, SO, SO2, NH and N-C1-4 alkyl; Y is H, halo, C1-4 (halo)alkyl, C1-4 alkoxy, C1-4 thioalkyl, etc.; Z is O and S; and their pharmaceutically acceptable salts thereof, are claimed. Example compound II was prepared by a multistep procedure (procedure given). All the invention compds. were evaluated for their GR inhibitory

activity. From the assay, it was determined that compound II exhibited IC50 value of 2.3 nM.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2006:1148723 CAPLUS [Full-text](#)

DOCUMENT NUMBER: 147:477019

TITLE: Multi-functionalized platinum(II) acetylides for optical power limiting

AUTHOR(S): Westlund, Robert; Malmstroem, Eva; Hoffmann, Markus; Vestberg, Robert; Hawker, Craig; Glimsdal, Eirik; Lindgren, Mikael; Norman, Patrick; Eriksson, Anders; Lopes, Cesar

CORPORATE SOURCE: KTH Fibre and Polymer Technology, Royal Institute of Technology, Stockholm, SE-100 44, Swed.

SOURCE: Proceedings of SPIE-The International Society for Optical Engineering (2006), 6401(Optical Materials in Defence Systems Technology III), 64010H/1-64010H/8 CODEN: PSISDG; ISSN: 0277-786X

PUBLISHER: SPIE-The International Society for Optical Engineering

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Preliminary results on the optical power limiting properties of Pt(II) acetylides containing triazole units are presented. The triazole units give a pos. contribution to the limiting abilities of the Pt(II) acetylide and this modified chromophore could have potential use in sensor protection devices. The versatile building block 2,2-bis(methylo)propionic acid (bis-MPA) can be used advantageously to functionalize nonlinear optical (NLO) Pt(II) acetylides. The bis-MPA units can be used to prepare dendritic substituents offering site isolation to the chromophore leading to improved clamping. The bis-MPA functionalization also improves the solubility of the Pt(II) acetylides in many organic solvents. The preparation of solid-state optical power limiters, where the NLO chromophore is inserted in an optically transparent matrix, is addressed. Again, the bis-MPA unit can be employed to increase the number of accessible end-groups to which matrix-compatible species can be attached. The hydroxy-functional Pt(II) acetylides can be modified to fit almost any matrix, organic or inorg. Finally, depending on functionalization, it is possible to prepare doped glasses where the chromophore is either embedded in the matrix, or covalently bonded to the matrix.

REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 5 OF 5 WPIX COPYRIGHT 2009 THOMSON REUTERS on STN

ACCESSION NUMBER: 2003-018783 [01] WPIX

CROSS REFERENCE: 2002-732863; 2002-750527; 2002-750528; 2002-759874; 2002-759875

DOC. NO. CPI: C2003-004563 [01]

TITLE: New compounds useful as metalloproteinase inhibitors for the treatment of conditions such as asthma

DERWENT CLASS: B03

INVENTOR: LEPISTO M; LEPISTOE M; MUNCK AF ROSENSCHOELD M; MUNCK AF ROSENSCHOELD M; MUNCK AF ROSENSCHOELD M; MUNCK A R M (ASTR-C) ASTRAZENCA AB; (LEPI-I) LEPISTO M; (ROSE-I) MUNCK AF ROSENSCHOELD M

COUNTRY COUNT: 99

PATENT INFO ABBR.:

| PATENT NO | KIND | DATE | WEEK | LA | PG | MAIN IPC |
|----------------|------|----------|-----------|----|--------|----------|
| WO 2002074752 | A1 | 20020926 | (200301)* | EN | 110[0] | |
| NO 2003004027 | A | 20031105 | (200380) | NO | | |
| EP 1370538 | A1 | 20031217 | (200402) | EN | | |
| BR 2002008062 | A | 20040302 | (200419) | PT | | |
| CZ 2003002498 | A3 | 20040317 | (200430) | CS | | |
| AU 2002237633 | A1 | 20021003 | (200432) | EN | | |
| SK 2003001091 | A3 | 20040504 | (200433) | SK | | |
| US 20040110809 | A1 | 20040610 | (200438) | EN | | |
| JP 2004527512 | W | 20040909 | (200459) | JA | 188 | |
| HU 2004000328 | A2 | 20040928 | (200470) | HU | | |
| MX 2003008187 | A1 | 20040201 | (200473) | ES | | |
| ZA 2003006738 | A | 20050223 | (200519) | EN | 117 | |
| NZ 528141 | A | 20050527 | (200537) | EN | | |
| RU 2293730 | C2 | 20070220 | (200752) | RU | | |
| AU 2002237633 | B2 | 20070405 | (200763) | EN | | |

APPLICATION DETAILS:

| PATENT NO | KIND | APPLICATION | DATE |
|----------------|------|----------------|----------|
| WO 2002074752 | A1 | WO 2002-SE479 | 20020313 |
| MX 2003008187 | A1 | WO 2002-SE479 | 20010313 |
| AU 2002237633 | A1 | AU 2002-237633 | 20020313 |
| BR 2002008062 | A | BR 2002-8062 | 20020313 |
| EP 1370538 | A1 | EP 2002-704038 | 20020313 |
| JP 2004527512 | W | JP 2002-573761 | 20020313 |
| NZ 528141 | A | NZ 2002-528141 | 20020313 |
| NO 2003004027 | A | WO 2002-SE479 | 20020313 |
| EP 1370538 | A1 | WO 2002-SE479 | 20020313 |
| BR 2002008062 | A | WO 2002-SE479 | 20020313 |
| CZ 2003002498 | A3 | WO 2002-SE479 | 20020313 |
| SK 2003001091 | A3 | WO 2002-SE479 | 20020313 |
| US 20040110809 | A1 | WO 2002-SE479 | 20020313 |
| JP 2004527512 | W | WO 2002-SE479 | 20020313 |
| HU 2004000328 | A2 | WO 2002-SE479 | 20020313 |
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| RU 2293730 | C2 | WO 2002-SE479 | 20020313 |
| CZ 2003002498 | A3 | CZ 2003-2498 | 20020313 |
| RU 2293730 | C2 | RU 2003-127736 | 20020313 |
| SK 2003001091 | A3 | SK 2003-1091 | 20020313 |
| ZA 2003006738 | A | ZA 2003-6738 | 20030828 |
| MX 2003008187 | A1 | MX 2003-8187 | 20030910 |
| NO 2003004027 | A | NO 2003-4027 | 20030911 |
| HU 2004000328 | A2 | HU 2004-328 | 20020313 |
| US 20040110809 | A1 | US 2004-471499 | 20040112 |
| AU 2002237633 | B2 | AU 2002-237633 | 20020313 |

FILING DETAILS:

| PATENT NO | KIND | PATENT NO |
|---------------|------|------------------------|
| EP 1370538 | A1 | Based on WO 2002074752 |
| BR 2002008062 | A | Based on WO 2002074752 |
| CZ 2003002498 | A3 | Based on WO 2002074752 |
| AU 2002237633 | A1 | Based on WO 2002074752 |
| SK 2003001091 | A3 | Based on WO 2002074752 |
| JP 2004527512 | W | Based on WO 2002074752 |
| HU 2004000328 | A2 | Based on WO 2002074752 |

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|---------------|----|----------|---------------|---|
| MX 2003008187 | A1 | Based on | WO 2002074752 | A |
| NZ 528141 | A | Based on | WO 2002074752 | A |
| RU 2293730 | C2 | Based on | WO 2002074752 | A |
| AU 2002237633 | B2 | Based on | WO 2002074752 | A |

PRIORITY APPLN. INFO: SE 2001-903 20010315

AN 2003-018783 [01] WPIX

CR 2002-732863; 2002-750527; 2002-750528; 2002-759874; 2002-759875

AB WO 2002074752 A1 UPAB: 20060118

NOVELTY - Substituted imidazolidine, oxazolidine or thiazolidine are new.

DETAILED DESCRIPTION - Compounds of formula (I) or their salts and in vivo hydrolysable esters are new.

X = NR1, O or S;

Y1 and Y2 = O or S;

Z = NR2, O or S;

m = 0 or 1;

A = e.g. a direct bond, alkyl or alkenyl;

R1 and R2 = H or (halo)alkyl;

R4 = e.g. H, alkyl;

R5 = a bicyclic or tricyclic group comprising 2 or 3 ring structures each of 3 - 7 ring atoms;

R3 and R6 = e.g. H, halo, alkyl, aryl.

Full definitions are given in the Definitions Field (Full Definitions).

An INDEPENDENT CLAIM is included for use of a compound of formula (I) or its in vivo hydrolysable precursor in the preparation of a medicament for the treatment of a disease or condition mediated by at least one metalloproteinase enzyme.

ACTIVITY - Antiasthmatic; Antiallergic; Antiinflammatory; Antirheumatic; Antiarthritic; Osteopathic; Antiarteriosclerotic; Vasotropic; Cytostatic; Cardiant; Gynecological; CNS-Gen.; Nootropic; Neuroprotective.

MECHANISM OF ACTION - Metalloproteinase (MMP) (preferably MMP12, MMP13, MMP9 and/or MMP8) inhibitor; Tumor necrosis factor inhibitor.

Test details are described, but no specific results for specific compounds are given.

USE - Compound (I) is used for the treatment of a disease or condition mediated by a metalloproteinase in a warm blooded animal (claimed), such as asthma, rhinitis, chronic obstructive pulmonary disease (COPD), arthritis (such as rheumatoid arthritis and osteoarthritis), atherosclerosis and restenosis, cancer, invasion and metastasis, diseases involving tissue destruction, loosening of hip joint replacements, periodontal disease, fibrotic disease, infarction and heart disease, liver and renal fibroids, endometriosis, diseases related to the weakening of the extracellular matrix, heart failure, aortic aneurysms, CNS related diseases (such as Alzheimer's disease and multiple sclerosis (MS)) and hematological disorders.

ADVANTAGE - The compounds exhibit improved potency, selectivity and/or pharmacokinetic properties. The compounds show an in vitro IC50 value of (0.1 - 10000, preferably 0.1 - 1000) nM.

=> d his nofil

(FILE 'HOME' ENTERED AT 10:45:11 ON 12 JAN 2009)

FILE 'REGISTRY' ENTERED AT 10:45:16 ON 12 JAN 2009

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L1      STR
L2      STR L1
L3      0 SEA SSS SAM L2
L4      1 SEA SSS FUL L2

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D SCA

FILE 'CAPLUS' ENTERED AT 10:49:47 ON 12 JAN 2009

E US2006-593543/APPS

L5 2 SEA SPE=ON ABB=ON PLU=ON US2006-593543/AP
D SCA TI

L6 1 SEA SPE=ON ABB=ON PLU=ON L5 AND TRIAZ?
SEL RN

FILE 'REGISTRY' ENTERED AT 10:51:17 ON 12 JAN 2009

L7 53 SEA SPE=ON ABB=ON PLU=ON (100-53-8/BI OR 100991-09-1/BI OR
1037628-17-3/BI OR 14001-66-2/BI OR 146480-36-6/BI OR 14874-70-
5/BI OR 16110-09-1/BI OR 177984-27-9/BI OR 177984-28-0/BI OR
252742-72-6/BI OR 260441-44-9/BI OR 26905-02-2/BI OR 2899-66-3/
BI OR 38212-33-8/BI OR 477904-80-6/BI OR 5382-16-1/BI OR
55444-67-2/BI OR 563-41-7/BI OR 64-04-0/BI OR 73901-41-4/BI OR
79099-07-3/BI OR 866602-59-7/BI OR 866602-60-0/BI OR 866602-61-
1/BI OR 866602-62-2/BI OR 866602-63-3/BI OR 866602-64-4/BI OR
866602-65-5/BI OR 866602-66-6/BI OR 866602-67-7/BI OR 866602-68
-8/BI OR 866602-69-9/BI OR 866602-70-2/BI OR 866602-71-3/BI OR
866602-72-4/BI OR 866602-73-5/BI OR 866602-74-6/BI OR 866602-75
-7/BI OR 866602-76-8/BI OR 866602-77-9/BI OR 866602-78-0/BI OR
866602-79-1/BI OR 866602-80-4/BI OR 866602-81-5/BI OR 866602-82
-6/BI OR 866602-83-7/BI OR 866602-84-8/BI OR 866602-85-9/BI OR
866602-86-0/BI OR 866602-88-2/BI OR 866602-89-3/BI OR 866602-90
-6/BI OR 9004-06-2/BI)

L8 23 SEA SPE=ON ABB=ON PLU=ON L7 AND N2CNC/ESS

L9 STR L2

L10 1 SEA SSS SAM L9

L11 35 SEA SSS FUL L9

FILE 'CAPLUS' ENTERED AT 11:00:54 ON 12 JAN 2009

L12 10 SEA SPE=ON ABB=ON PLU=ON L11

FILE 'REGISTRY' ENTERED AT 11:01:11 ON 12 JAN 2009

L13 STR L9

L14 5 SEA SUB=L11 SSS FUL L13

L15 STR L13

L16 0 SEA SSS SAM L15

L17 0 SEA SUB=L11 SSS FUL L15

L18 15 SEA SPE=ON ABB=ON PLU=ON L11 AND L7

FILE 'CAPLUS, DISSABS, CONFSCI, WPIX' ENTERED AT 11:04:29 ON 12 JAN 2009

L19 496 SEA SPE=ON ABB=ON PLU=ON ERIKSSON A/AU OR ERIKSSON ANDER?/AU

L20 38 SEA SPE=ON ABB=ON PLU=ON LEPISTO M/AU OR LEPISTO M ?/AU OR
LEPISTO MATT?/AU

L21 613 SEA SPE=ON ABB=ON PLU=ON L19 OR ERIKSSON A ?/AU

L22 643 SEA SPE=ON ABB=ON PLU=ON (L20 OR L21)

L23 7 SEA SPE=ON ABB=ON PLU=ON L22 AND TRIAZOL?

FILE 'CAPLUS' ENTERED AT 11:05:54 ON 12 JAN 2009

D QUE L12

D L12 IBIB ABS HITSTR TOT

FILE 'CAPLUS, DISSABS, CONFSCI, WPIX' ENTERED AT 11:06:19 ON 12 JAN 2009

D QUE L23

L24 5 DUP REM L23 (2 DUPLICATES REMOVED)

ANSWERS '1-4' FROM FILE CAPLUS

ANSWER '5' FROM FILE WPIX

D L24 IBIB ABS TOT